



BioTimes®



EMSLAND GROUP AND NOVOZYMES
– COLLABORATING TO CREATE A LOW-ACRYLAMIDE FUTURE

Novozymes is the world leader in bioinnovation. Together with customers across a broad array of industries we create tomorrow's industrial biosolutions, improving our customers' business and the use of our planet's resources.

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IMPROVING BIOTIMES – READERS HAVE A SAY

Last year many of you took part in a survey designed to gain reader feedback so that we could improve our *BioTimes* offering. Response on the printed magazine was overwhelmingly positive, though many commented that we could improve the *BioTimes* website. We have now launched a new website to better meet our readers' needs.



"We had a feeling that readers really enjoyed *BioTimes*, but we wanted it confirmed, so we created the feedback survey," says Susanne Strand, *BioTimes*' editor. "And we wanted to know how we could improve the content and design of the magazine."

According to readers, there is not much they want improved about *BioTimes*. They like the look of the magazine, the mix of subjects, as well as the writing. In fact, most do not want any changes to the printed version of the magazine. But quite a few commented that the current website did not function optimally and should be improved.

And so it has been.

A change for the better

"We took readers' feedback to heart and I'm happy to say we're now launching a completely new *BioTimes* website," says Susanne Strand. "We've changed nearly everything

about the old website – the design, the functionality – the only thing that we haven't changed is the quality and the range of the articles we publish."

With the launch of the new website readers can look forward to a better-looking and more interesting site and one that is much easier to navigate. Improvements readers can now enjoy include:

- Improved search so that specific articles can be found quickly and easily
- E-mail notifications that give access to articles as soon as they are published
- Links to related content so that complementary information can be found with just one click

"Readers have opened our eyes to the possibilities that we need to embrace on our website," says Susanne Strand. "We have updated our *BioTimes* strategy, and the launch of the new website is just the first step in a long journey to offer our readers an interesting and valuable online reading experience. Readers can look forward to future initiatives that will give them even more possibilities to learn about our biotechnology online." ■

BioTimes®

VISIT BIOTIMES AT WWW.BIOTIMES.COM

Do not forget to sign up for e-mail notifications, so that you are always one of the first to know what is going on in the world of bioinnovation.



REACH – EXTENDING TO A BETTER ENVIRONMENT

It has been called the most important EU legislation in 20 years, yet the word instills concerns in many industry players across all of Europe. For most people “reach” means to extend out as far as possible, but in the world of chemicals the word has got a new meaning the last couple of years.

The EU’s REACH stands for Registration, Evaluation, Authorisation and Restriction of Chemicals. The acronym is self-explanatory but another 10,000 pages of guidelines thoroughly explain what the new piece of legislation really means. In a nutshell it is a new chemical legislation with the main objective to ensure that the chemical business uses chemicals in a way that is safe to humans and the environment. The legislation concerns all industries, approximately 29,000 companies, producing or importing chemicals in the EU. About 30,000 of the estimated 100,000 chemicals in Europe are covered by REACH.

Enzymes are regarded as chemicals by authorities although most people might not consider them as such. “All substances in the

EU have to be registered under REACH unless there are specific exceptions. Technical enzymes, ranging from the detergent, textile, leather, forest product, and cosmetic industries to the fuel ethanol industry, fall under the new law,” says Rie Tsuchiya, Regulatory Affairs Manager at Novozymes.

The main feature of REACH, compared to the former bundle of some 40 regulations, is that it shifts the responsibility for providing safety documentation on to the producer. “The EU’s principle ‘no data – no market’ puts a great responsibility on the producer. At Novozymes we already carry out extensive data collection on how enzymes affect humans and the environment. We’re now complementing these data to fit the new requirements,” says Rie Tsuchiya.



FACTS ON REACH

REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
Scope	<ul style="list-style-type: none"> • 10,000 pages of text • 30,000 chemicals to be registered over 11 years
Cost	<ul style="list-style-type: none"> • The European Commission estimates REACH will cost the industry EUR 2.8–5.2 billion • The Commission estimates to save EUR 54 billion in healthcare costs as the exposure to dangerous chemicals is reduced
Process	<ul style="list-style-type: none"> • REACH entered into force on June 1, 2007. It requires basic safety data on every chemical in the EU and will restrict any substance deemed to endanger health or the environment. All businesses importing or manufacturing more than 1 ton of chemical substance per year had to preregister between June 1 and December 1, 2008. Companies that have filed a preregistration document for a chemical can continue producing or importing that substance without completing formal registration until November 2010, May 2013, or May 2018. The deadline depends on how much of the substance they manufacture or import, with the earliest deadline for higher production compounds and for chemicals with demonstrated toxicity





SAVE TIME AND MONEY

► Tough times for harsh chemicals, good times for enzymes

REACH encourages the industry to seek alternatives to harsh chemicals. To use “substances of very high concern” under REACH, companies have to apply for a special permit and pay an authorization fee of EUR 50,000. “Enzymes substitute harsh chemicals in many processes, and the legislation focuses on finding more environmentally friendly alternatives. We believe enzymes will receive an even more prominent role as chemical substitutes,” says Rie Tsuchiya.

REACHing the goal

At Novozymes a cross-organizational project group has worked since May 2007 to establish good networks and relationships with collaborating organizations, developing industry standards for safety documentation, and internally ensuring that all involved stakeholders are well informed. “We’ve worked closely with our suppliers and customers to inform them about the implications of REACH. We’re also the driving force, working in consortium with our competitors, to produce various industry guidelines and policy documents,” says Rie Tsuchiya.

The project group assesses and manages all relevant aspects of REACH, including the technical guidance documents associated with REACH. It draws on expertise from people from many of Novozymes’ business areas, including Regulatory Affairs, Legal, Sales, Product Safety, and Toxicology.

“We believe REACH has great potential in the long run as focus shifts to safe and sustainable chemicals. The foundations of REACH are certainly in line with Novozymes’ biotechnology base and business strategy. REACH will therefore indirectly support Novozymes’ efforts to maintain and grow our existing business, and develop new enzymes and other biobased products,” says Karin Weinell, Senior Manager for the REACH project at Novozymes. ■

The machines are running full-speed at PT. Kemilau Warna Ceria’s factory in Java, Indonesia. Producing textiles means using large amounts of water, electricity, and chemicals. Novozymes’ Cellusoft Combi combines three processes into one, saving costs and production time without affecting the quality of the fabric.

About 85% of the water in textile production is used predominantly for dyeing and finishing. These processes use about 75% of all the energy and 65% of the chemicals to convert fiber into textile. Any cut in production time, chemical, energy, and water usage means substantial cost savings for textile mills constantly working with tight cost margins. It also washes away much of the industry’s bad reputation as a great industrial polluter.

So far enzymes have been helpful in this respect both during bleach clean-up and biopolishing. Mills traditionally bleach to obtain smashing colors in the dyeing process. The bleach is normally rinsed with reducing agents and large amounts of hot water. By adding a small amount of catalase in the bleach clean-up process hydrogen peroxide is catalyzed into oxygen and water, resulting in lower water usage and less wastewater pollution.

To get smooth cotton textiles with vibrant colors, textile mills polish the fabrics, targeting the small protruding fiber ends that make the fabric look fuzzy and create pills. Polishing can be done by singeing with a gas flame. The less harsh alternative, biopolishing, uses cellulases to polish the yarn surface and prevent pilling.

Get two for one

To optimize the processes and offer an environmentally friendly alternative, Novozymes has developed a product that combines bleach clean-up and biopolishing into one. “Cellusoft Combi greatly reduces time, energy, and water consumption by combining biopolishing and bleach clean-up processes in the dyeing step. The product allows end user mills to free up production and improve throughput,” says Umar Riaz, Global Marketing Manager for textiles at Novozymes.

At PT. Kemilau Warna Ceria, they have tried to biopolish with Cellusoft Combi. The 1,600 employees produce 13,000 meters woven fabric and 20,000 kg knitted fabric a day for dyeing and printing. The company has recently made large investments to develop a high-quality knitted fabric and has already invested in several new machines to improve capacity. To boost production further the director of PT. Kemilau Warna Ceria, Hendro Prasetyo, decided to try out the ready-to-use Cellusoft Combi. The first test results were promising. “We find the product very good, both technically and concept-wise. Cellusoft Combi reduces processing time and saves costs

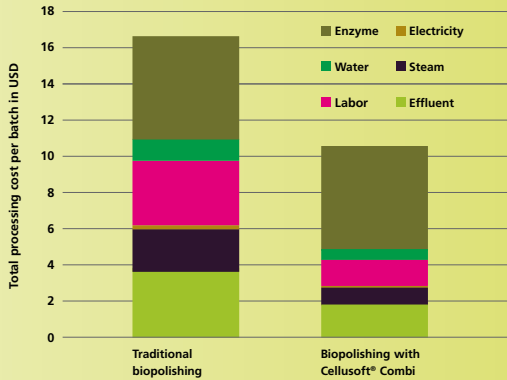
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WITH CELLUSOFT® COMBI

We want smooth, soft, high-quality textiles for our everyday clothes. Biopolishing with Cellusoft® Combi makes this possible at an affordable price.

SAVINGS ON BIOPOLISHING WITH CELLUSOFT® COMBI



Cellusoft® Combi can save the mill energy, time, and resources compared to traditional biopolishing products.

on electricity, water, and steam,” says Hendro Prasetyo. Experts in the company were equally positive about the results. “Cellusoft Combi removed hydrogen peroxide from the fabric very well, and the biopolishing was excellent,” says Sukardi, head of the dyeing department at PT. Kemilau Warna Ceria.

Time is money

So far one of the greatest hurdles for using enzymes is that it introduces an extra step in the production. “Mills currently doing biopolishing and bleach clean-up in two separate processes now have the opportunity to combine both steps during dyeing in an economical way. Due to the unique nature of Cellusoft Combi, it doesn’t interact with dyes and improves fabric quality, while saving the mill up to 100 minutes in processing time, plus water, labor, and energy costs,” says Umar Riaz.

The great savings that Cellusoft Combi gives create great interest in a competitive market. “A majority of our customers who’ve tested the product have now replaced the traditional acid cellulases with unique Cellusoft Combi,” says Han Kuilderd, Customer Solutions Manager for textiles at Novozymes. “Companies that biopolish with Cellusoft Combi can produce a high-quality fabric at virtually the same cost as fabrics that aren’t biopolished but still achieve the smoothness and softness that biopolished fabrics are known for. It’s simply a win-win product.” ■



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A HEALTHY PARTNERSHIP FOR A HEALTHY EARTH

LCA DEFINED

Lifecycle assessment (LCA) is an environmental management tool, which is used to assess environmental impacts of products and services in their entire lifecycle, from "cradle to grave," that is, from raw material extraction, through production and use, to final disposal or recycling.

Palm oil is used to produce margarine hardstock which is a critical ingredient in the margarine that we eat every day.



The palm oil industry has been accused of contributing to deforestation, but there are many ways to make it less of a threat. Unilever is a firm driver of sustainable palm oil sourcing and is working with Novozymes to ensure that the entire margarine hardstock process is environmentally sound.

Around three quarters of the world's oil palm is grown in Indonesia and Malaysia, often on peat land and in tropical rain forest. The clearance and burning of Southeast Asia's peat forests release 2 billion tons of greenhouse gases every year. According to some estimates, deforestation in Indonesia alone accounts for 4% of global greenhouse gas emissions – making it the third highest emitter behind the US and China.

Global consumer goods manufacturer Unilever is committed to sustainable palm oil sourcing according to the Roundtable Sustainable Palm Oil (RSPO) principles and criteria. The company shares the concerns of many organizations and consumers regarding the destruction of rain forest and supports a request for a moratorium against deforestation. But Unilever's concern stretches beyond just the sustainable sourcing of palm oil, into sustainable production of all oils and fats for use in consumer products.

Unilever uses palm oil, often after modification, in many food as well as nonfood products. So sustainability is not just an issue of sourcing, but how the palm oil is used and prepared for incorporation into final products.

"Cooperation with Novozymes started with early research into fat modification which is now being implemented for the production of margarine hardstock," says Gerrit van Duijn, Oil Supply Technology Director at Unilever.

Margarine hardstock is a critical ingredient in margarine, determining the physical properties of the product, such as firmness, spreadability, and mouthfeel.

Improving sustainability together

Novozymes has carried out a number of lifecycle assessments (LCAs) to document the benefits of replacing chemicals with enzymes in various processes. Together with Unilever, Novozymes

investigated the environmental benefits realized if margarine hardstock was produced by enzymatic rather than chemical interesterification.

"This process required that the two organizations exchanged information so that a full and accurate LCA could be made," says Jesper Hedal Kløverpris, LCA specialist at Novozymes. "The results showed clear benefits of switching to enzyme technology."

This collaboration was important for a number of reasons. Firstly, an accurate LCA can only be made if correct data are used. While Unilever knew a great deal about chemical interesterification, they did not have as much knowledge about the enzyme production and application. Secondly, the resulting data could be used by Unilever to show its suppliers how they could contribute to Unilever's goals of sustainable production. Not just to improve how they sourced their raw materials but also how they could perform sustainably further down the supply chain as well.

"The success of this collaboration and the use to which Unilever is putting the results are a prime example of how other companies can work with Novozymes to improve the sustainability and efficiency of their own processes," says David Cowan, Customer Solutions Scientist at Novozymes. ■

Oil palm trees supply palm oil for use in manufacturing a wide range of food and nonfood consumer products.



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READ MORE

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ONE, TWO... EIGHT ENZYMES IN ONE DETERGENT

Two proteases, two amylases, two cellulases, one lipase, one mannanase, all in one detergent formulation – Danlind’s Total is the world’s first detergent with eight different enzymes. Danish consumers can now pick up Total as a powder, liquid, or laundry tablet for both whites and colors from the shelves of a Dansk Supermarked store.



TOTAL – LET ENZYMES DO THE WORK

THE ENZYMES INCLUDED IN TOTAL ARE:

- Polarzyme®** A protease for efficient stain removal and cleanliness at low temperatures.
- Ovozyme®** A protease specifically engineered to resist protease inhibitors in eggs. Highly efficient at low dosages.
- Termamyl®** An amylase for robust starch removal and whiteness and high performance at medium to high temperatures.
- Stainzyme®** A third-generation amylase for high-performance removal of the most challenging starch-based stains. Efficient at low temperatures and short cycles.
- Lipex®** A lipase for effective fatty stain removal during the first wash, ensuring in-depth cleaning by removing fatty soils lodged between textile fibers.
- Celluzyme®** A robust cellulase under demanding wash conditions, delivering general cleaning and fabric care.
- Celluclean®** A cellulase that provides superior whitening maintenance and anti-graying effects while preserving brightness in colored and contrasts in striped clothes.
- Mannaway®** A mannanase for removal of mannan stains, offering in-depth cleaning.

Total is on the verge of being a success story like Danlind’s cold-wash product CARE®, which entered the market as a cold-wash detergent a few years ago. Based on the same formulation as CARE, Total kicks it up a notch and goes from containing four enzymes to eight.

“The reason for using so many enzymes was to boost performance. When we came out with CARE, all our claims were green and now we have mechanical claims that have to do with giving consumers the best cleaning, smell, and whiteness,” says Dorthe Lund, Sales Manager at Danlind.

Bioinnovate the old detergent

The formulation base used to develop Total was reformulated to contain no phosphates, new surfactant and builder systems, and enzymes to ensure satisfactory wash performance at low wash temperatures.

“We’re setting a world record here,” says Claus Ladefoged, Senior Account Manager at Novozymes. “Total confirms that you can replace chemical ingredients with a multienzyme solution

without compromising performance. I believe Total will show other detergent manufacturers that adding more enzymes to their formulations is the way forward for the detergent industry.”

Stains are complex

The stains that keep consumers up at night today are different from the stains that plagued us 20 or even 10 years ago. Stains are less motor oil based and more food based as consumers are eating more partially or fully manufactured foods that usually contain thickeners.

“With Total we wanted to boost the overall performance and also show effect on new types of stains that can be removed by enzymes,” says Henrik Jørgensen, Laboratory Manager at Danlind and the brains and brawn behind Total.

“Mannaway® is of interest here as it takes care of stains from chocolate ice cream, baby food, desserts, thickeners, and other such food products. Celluclean® is part of the formulation because it prevents backstaining, especially on polyester fabrics, and improves overall whiteness.”

Totally impressive

Total is advertised by Dansk Supermarked to be tough on stains and easy on the nose. Danlind and Dansk Supermarked have been candid about the source of the high performance of Total by listing all eight enzymes and their benefits on the packaging itself.

“We appreciate the value of the Novozymes brand in ensuring consumers that Total is an efficient detergent, containing what we believe are the best enzymes on the market,” says Ilse Corneliussen Skannerup, Product Manager for Washing and Cleaning, Dansk Supermarked. “The mix of eight enzymes is a perfect match to what Total stands for – the idea that whatever the washing problem might be, Total is expected to solve it.” ■

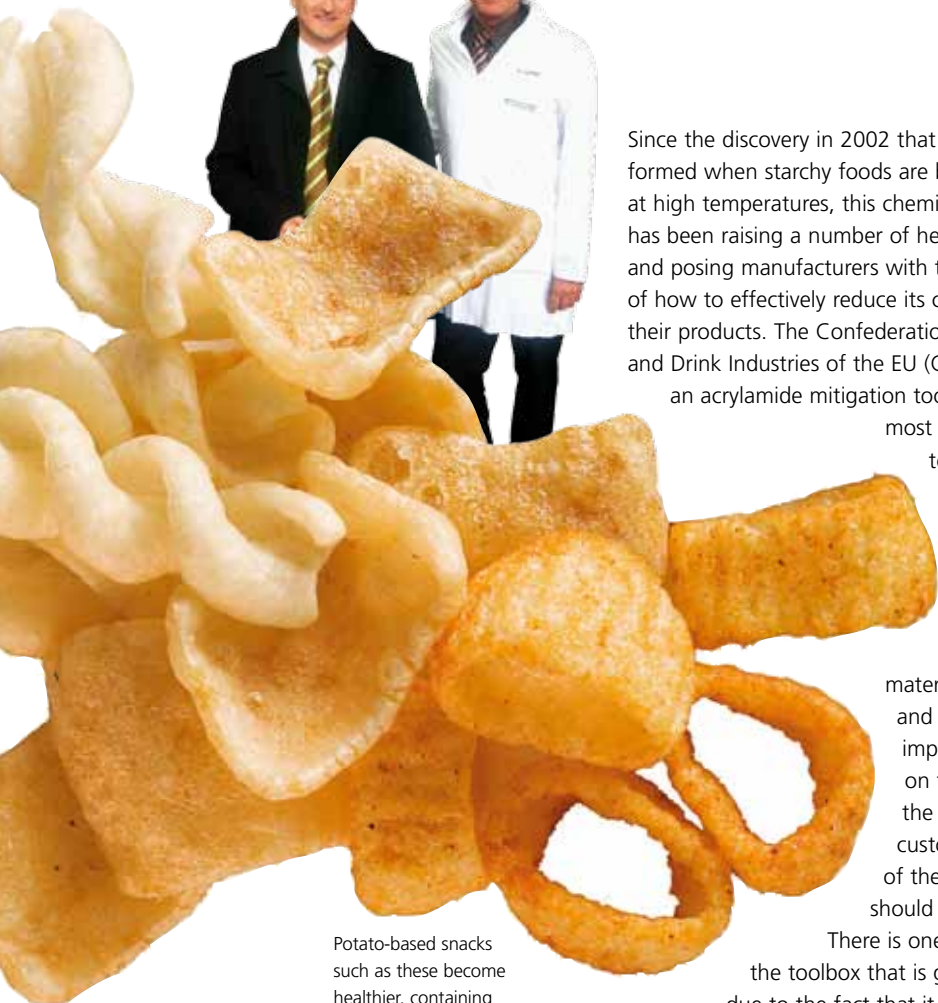
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INNOVATION AND ENZYMES AT EMSLAND GROUP



Sylvain Laperche, Account Manager at Novozymes (left), with Emsland Group's Wolfgang Lippke, head of Emsland Group's Food R&D department.



Potato-based snacks such as these become healthier, containing approximately 60% less acrylamide, when produced using Acrylaway®.

Emsland Group, the largest potato starch producer in Germany and global leader in the production of starch-finishing products, potato protein, flakes, and granules, adds value to its products and offers a new level of support to customers by using enzymatic innovation to reduce the level of asparagine, a precursor of acrylamide, in its potato granules.

Since the discovery in 2002 that acrylamide is formed when starchy foods are baked or fried at high temperatures, this chemical substance has been raising a number of health concerns and posing manufacturers with the challenge of how to effectively reduce its concentration in their products. The Confederation of the Food and Drink Industries of the EU (CIAA) launched an acrylamide mitigation toolbox to offer the most efficient solutions to assist the affected industries.

The toolbox is a combination of suggestions for changes in raw materials, processes, and recipes, with importance placed on the fact that the brand-specific customer acceptance of the final products should not be impacted.

There is one option within the toolbox that is growing in appeal due to the fact that it does not influence the final product's taste or appearance. This innovative enzymatic technology is offered by asparaginases such as Novozymes' Acrylaway®. And Emsland Group, with its corporate slogan being "using nature to create," was the perfect collaboration partner to help bring Acrylaway to commercial success in the production of potato granules.

Health and taste appeal

Although Acrylaway was launched in 2007 to customers manufacturing dough-based products due to the initial ease of application, recent trials have shown that reductions in acrylamide content of up to 80% are possible in the production of French fries, with additional impressive results demonstrated in the field of potato-based snacks. Emsland Group's pioneering industrial trials resulted in a 60% asparagine reduction in potato granules and above 60% acrylamide reduction in snacks produced from its treated potato granules – and this impressive result has the potential to be further improved if the snack producers also implement an acrylamide-reducing technology before baking or frying their snacks. What is truly appealing about Acrylaway is that the reduction of acrylamide in these food types is achieved without altering the tempting flavor or visual aspect of potato-based snacks – a sizable bonus for food manufacturers that are searching for acrylamide-reducing solutions and worry about the continued allure of their products for consumers.

Consistent collaboration leads to results

"Stable quality is a key requirement for our customers," says Wolfgang Lippke, head of Emsland Group's Food R&D department. "As an innovative company we wanted to work closely with our customers and react quickly to concerns about acrylamide while at the same time providing them with the reliable supply of high-quality potato granules they expect from us. And our relationship with Novozymes and the use of Acrylaway enabled us to do exactly that."



Potatoes – the key ingredient in Emsland Group’s production plant.

BACK TO BASICS

The main mechanisms that cause the formation of acrylamide are commonly found in starchy foods – reducing sugars and the amino acid asparagine. During the baking or frying stage, a process called the Maillard reaction or nonenzymatic browning occurs – essential for important color and flavor developments in baked, fried, and toasted foods. Through a cascade of reactions, the side chain of asparagine is converted into acrylamide. As Emsland Group does not expose its potato granules to extreme heat, these do not contain acrylamide. By treating the granules, Emsland Group offers its customers a product that contains a reduced level of asparagine, a precursor of acrylamide, when it uses heat to transform the granules into potato snacks.

The Novozymes/Emsland Group collaboration began in 2005, starting with discussions that evolved into early lab trials. “Both Hanne Vang Hendriksen, Senior Scientist at Novozymes, and Peter Müller, Application Manager for the Food and Nutrition division at Novozymes, have been exceptional resources for us,” continues Wolfgang Lippke. “We enjoy an excellent exchange of information, and although we never disclose customer information, we always ensure our communication is aligned with Novozymes.” The close interaction between both companies continued, experimenting with factory trials using both Acrylaway-treated and untreated potato granules until a satisfactory reduction in the level of acrylamide was achieved in final snack products.

With enhanced results, Emsland Group was ready to reveal its improved potato granules to its customers and this led to the inclusion of Acrylaway into its production plan in 2008. “We’re extremely satisfied with our relationship with Emsland,” says Emmanuel Michelot, Regional Marketing Manager for Novozymes’ Food and Nutrition unit. “Together we can help the potato-processing industry to solve the problem of acrylamide. Our aim is to eventually cover all product areas that are affected by acrylamide, and similar collaborations with major players in these markets will be key to continuing toward our goal of making food safer and healthy.”

Concern invites innovation

Although the potential risk to humans by dietary exposure to acrylamide is not yet fully known, an increasing number of studies is currently in progress at an international level to collect the data needed to make an informed evaluation. Until more results are available, JECFA, the Joint FAO/WHO Expert Committee on Food Additives, has recommended that appropriate efforts should be made to reduce the concentration of acryl-

amide in food. In Germany, a strategy to minimize the acrylamide content in foodstuffs was agreed among the Federal Office of Consumer Protection and Food Safety (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit – BVL), the German federal states, the industry, and the Federal Ministry of Consumer Protection, Food and Agriculture. This involves the BVL collecting analytic results on the acrylamide contents in foodstuffs and assigning a signal value for each food group based on these data.

Food control authorities contact the producers of foodstuffs that exceed the signal value and help assess whether their processes or ingredients can be altered to reduce the level of acrylamide. “Acrylamide reduction is a big issue in Germany at the moment,” confirms Wolfgang Lippke. “Customers actually approached us, asking us if we were doing anything that could help them reduce the acrylamide content of their snacks. Some had even started to develop solutions for themselves based on the CIAA toolbox.”

As Emsland Group’s products do not contain acrylamide, they are not under any obligation to invest in this change. But a company with a conscience such as Emsland Group has a goal to produce healthy products from healthy raw materials and wants to support its customers through adding unique value to its granules.

The perfect fit

The Emsland Group/Novozymes collaboration is a carefully considered one, combining a solution that truly works with a receptive company that wants to add value to its products and enhance its recognition as a supplier. “Although there are other technologies to reduce acrylamide, asparaginases such as Acrylaway are the only solution that doesn’t alter the quality of the final product,” says Sylvain Laperche, Account Manager, Novozymes Food and Nutrition. “It’s also afford-

able – while adding significant value to the final product.”

“Acrylaway really works for us,” explains Wolfgang Lippke. “The enzyme technology matches our process perfectly – the temperature and holding time that are optimal for Acrylaway were already part of our process. We do the work, so our customers don’t have to change their equipment, processes, or worry about dosage.”

A low-acrylamide future beckons

Today’s consumers are conscious and cautious about what they eat. Health and food quality are major drivers for the market right now, and food safety is a key consumer concern. It is a request from the society that our food is not only tasty and of high quality, but also safe and healthy – and in countries such as Germany, this requirement is supported by the government. Innovative enzymatic solutions such as Acrylaway and progressive companies such as Emsland Group ensure that acrylamide levels are reduced in potato-based snacks, without altering the taste and appearance of these products. By achieving this, they help to produce safe and healthy food that benefits consumers, society, and food manufacturers. ■



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CHINESE DISTILLERS FOCUS ON SAVING ENERGY



Traditional high-temperature cooking in Chinese distilleries requiring excessive steaming is being replaced by a milder process in a jet cooker using the new liquefaction enzyme Liquoflow®.



High energy prices have increased costs for Chinese beverage alcohol producers using the traditional high-temperature

cooking process. Enzymatic liquefaction technology for jet cooking at lower temperatures using Novozymes alpha-amylases is offering them a way to save energy and also reduce raw material consumption.

Alcohol made by fermentation is a traditional industrial product in China. The production process and equipment are quite dated as many of the distilling plants are old. Today, many producers are looking for an improved process.

Challenging times

With high grain and energy prices, the distilling industry is facing some tough challenges nowadays. At the same time, the national and local governments are strictly implementing energy conservation policies to reduce energy consumption. Some medium- and small-scale producers with dated production equipment and processes are feeling the pinch, especially in comparison to the large modern distilling plants that have been built in China recently.

Under the mounting pressure of industrial competition and tough regulations, it is imperative that processes are optimized, the use of raw materials is maximized, and energy consumption is minimized.

A few Chinese alcohol producers have the advantage of using cheap local coal resources for the traditional high-temperature cooking process. Nevertheless, even for them, there are more and more disadvantages associated with this process.

High priority: lower energy

Coal and oil are finite resources with fluctuating prices, and their combustion leads to global warming. China is urgently looking to reduce its energy consumption and carbon footprint. Therefore the Chinese authorities responsible for various industries have introduced a series of policies and measures to direct producers toward technology that can save energy.

As Chinese distillers are looking for ways to lower their energy consumption, Novozymes in China has been actively proposing the use of jet cooking at medium temperatures.

One prime area where Novozymes has been active is in the Jiaozuo region of Henan Province where the plants use traditional high-temperature steaming. Large amounts of steam are required to ensure that the starch derived from corn is completely hydrolyzed. The process takes a long time and this leads to losses of starch, which in turn result in less fermentable sugars and lower yields

of alcohol. Not only is the raw material conversion rate lower but the production cost is higher. In addition, the high temperatures and high pressure increase wear and tear on equipment, shortening its productive lifetime. Now these producers are looking for alternatives.

Better alcohol and DDGS

Huaxing Distillery has a total production capacity of 180,000 million tons per year and is the largest beverage alcohol producer in the Jiaozuo region and the second largest producer in Henan Province. This was one of the first companies to do trials with medium-temperature jet cooking. The trials were conducted in September 2008 with the assistance of the Novozymes Beverage Alcohol industry Customer Support and sales teams in China.

"We assisted them to optimize their current process," said Changping Sun, a Customer Solutions Application Scientist with Novozymes

"The use of alpha-amylases for the jet cooking liquefaction application has been accepted by the Chinese alcohol producers and is now a trend in the industry."

Changping Sun, Customer Solutions Application Scientist with Novozymes China





Liquoflow® is a new solution from Novozymes that effectively increases alcohol output as well as savings in water and energy.

China. “Liquoflow was successfully applied in their production and they were able to decrease the temperature of jet cooking from over 120 °C to 100–105 °C. After two months of continuous full-scale production trials, the energy and water consumption decreased significantly and the quality of the distillers dried grains with solubles – or DDGS – greatly improved.”

Now Huaxing Distillery has switched to the new process with Liquoflow.

New liquefaction enzyme

Liquoflow is a new liquefaction enzyme from Novozymes that increases ethanol output as well as giving savings in water and energy. Depending on the needs of a distiller, Liquoflow can help them to focus on High Gravity Fermentation (HGF), maximize the use of back stillage, and optimize preliquefaction and liquefaction.

Liquoflow offers superior viscosity reduction, helping distillers to achieve increased dry solids and HGF. It is a robust enzyme that gives optimal liquefaction within a wide pH range (5.2–6.0). There are therefore no problems with liquefaction at the very low pH of 5.2.

The typical liquefaction conditions when using Liquoflow are to jet cook at 100–105 °C followed by dextrinization for 1 hour at 85 °C.

“More cost-effective”

Wen Hongjun, who is Technical Director at

Huaxing Distillery, commented: “We succeeded in implementing a medium-temperature liquefaction and saccharification process in two jet cookers thanks to our cooperation with Novozymes. In comparison to various alpha-amylases that we’ve tested, the performance of Liquoflow from Novozymes is perfect for us. Liquoflow is suited to our current production system and does what other alpha-amylases on the local market can’t achieve. In addition, the dosage of Liquoflow is very low, and it offers good performance at low pH. We’ve calculated the cost and found that it’s more cost-effective than previous liquefaction enzymes. It not only improved our production efficiency but also the quality of our DDGS. This new DDGS is much preferred by our customers.

“The CEO and management team have decided to introduce Novozymes enzymes for the medium-temperature jet cooking liquefaction process. We foresee that we’ll continue to cooperate with Novozymes in the future to support us in our efforts to improve alcohol output and reduce costs.”

This trial confirms the results from other production trials in China where clear differences were observed in the quality of the alcohol and DDGS. The taste of the alcohol improved and the DDGS feed by-product from enzymatic liquefaction had a golden color, an attractive odor, and a higher protein content. The high-temperature steaming cooking process produces DDGS that is

black in color and has a burnt odor and a lower protein content. Therefore the price is much lower and there is less demand from the animal feed market.

Changping Sun added: “The use of alpha-amylases for the jet cooking liquefaction application has been accepted by the Chinese alcohol producers and is now a trend in the industry. The advantages are obvious, in particular the energy savings with the HGF process we’re proposing. We continue to improve the process.”

Huaxing Distillery acted as a catalyst of change for other alcohol producers in China. After its success, other producers in Henan Province contacted Novozymes and requested technical support to try the new enzyme application. Meanwhile Novozymes is cooperating with Huaxing Distillery to optimize its production process and improve the performance of liquefaction with Liquoflow even further. ■

Editor’s note: Sadly Changping Sun recently passed away after the writing of this article.

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NOVODIESEL – THE NEXT BREAKTH

Chemical methods of biodiesel production are most prominent in the world today, but the technological, economic, and sustainability advantages of enzymatic biodiesel production are extensive.

Jesper Brask, Per Munk Nielsen, and Hans Christian Holm believe in the benefits of producing biodiesel using enzymes and are working hard to make the technology widely available.



THE SUSTAINABLE BIODIESEL PROJECT

Biodiesel made using enzymatic transesterification with ethanol instead of methanol has been suggested as a cleaner, more sustainable alternative. And enzymatic biodiesel production has many advantages over its chemical counterpart:

- It works well with fluctuating raw material quality
- It needs fewer processing steps
- It produces higher-quality glycerol (a valuable coproduct)
- It uses less energy and generates less wastewater

Due to these significant benefits, more and more research is being done in the field, and a viable, sustainable solution is well within reach.

From FAME to FAEE

Today, commercial biodiesel is fatty acid methyl esters (FAME), which is made with methanol.

Methanol works well in a chemically catalyzed process, and more importantly, it is a cheap type of alcohol in most regions. But with increased global bioethanol production, any price advantage over ethanol could soon change.

Ethanol is the preferred alcohol for the enzymatic process, resulting in fatty acid ethyl esters (FAEE). Ethanol is a larger and heavier alcohol than methanol which means a mass yield gain of the FAEE biodiesel. This mass yield gain means that more biodiesel is made from a unit of oil in the enzymatic ethanol process than in the chemical methanol process.

“Ethanol is already sold at prices lower than methanol in certain countries such as Brazil,” says Hans Christian Holm, Global Marketing Manager at Novozymes. “Since the alcohol component is always significantly cheaper than

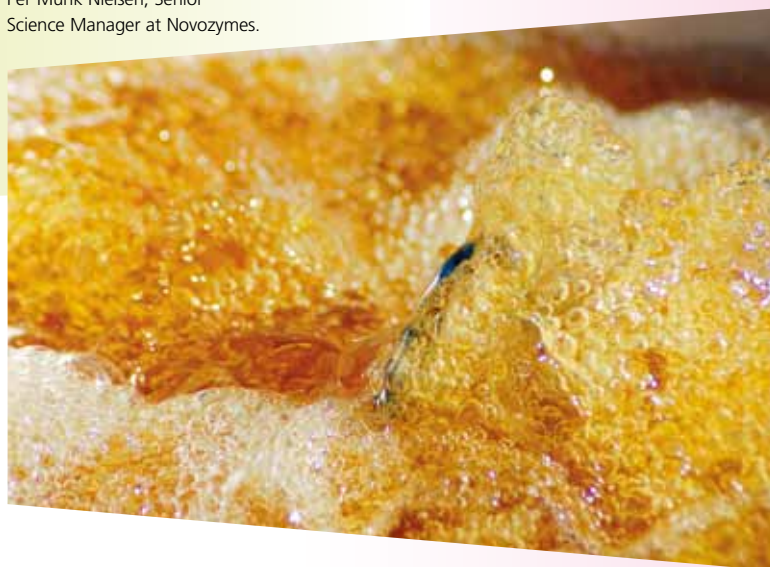
An EUR 2.4 million grant contract from the Danish National Advanced Technology Foundation (HTF) was given in late 2008 to a project consortium to establish a world-leading enzyme technology for the next generation of biodiesel production. The project will take place over the next three years and the goal is to develop and document a biodiesel process that is cost-effective and environmentally superior to chemical transesterification. Complete documentation of the process including a quantitative sustainability assessment is also within the project's scope.

The project is formed as a consortium of Danish companies and academic groups, including Novozymes, Emmelev – a Danish biodiesel producer – the University of Aarhus, and the Technical University of Denmark.

the oil component, the extra volume gain when using ethanol instead of methanol could become a major sales argument, particularly for the Brazilian market.”

ROUGH IN REDUCING CO₂ EMISSIONS

“Enzymatic biodiesel production using bioethanol and waste oils could become a ‘green-green’ biodiesel for the future,” says Per Munk Nielsen, Senior Science Manager at Novozymes.



Added to this, the chemical ethanol process is troubled with technical issues, giving further advantage to the enzymatic ethanol process.

Moving to lower-quality feedstocks

The fundamental advantage of an enzymatic biodiesel process is that triglycerides (and partial glycerides) as well as free fatty acids (FFA) can be efficiently transformed into biodiesel under the same mild conditions. By selecting the right enzyme composition, it is possible to make a continuous single-step process, even with very high FFA content in the oil. This allows the use of low-quality and nonfood oils without a negative impact on the environment.

The choice of feedstock for today’s commercial biodiesel plants depends largely on geography, with rapeseed oil dominating in the EU, soybean oil in the US and Latin America, and palm oil in Asia. These oils can easily be used as feedstock for enzymatic biodiesel production. Already today, research shows that this is a possibility with practically all the known plant oils. But the greatest benefits of enzymatic treatment can be obtained with low-cost, low-quality oils with high FFA content. These types of oils include animal fat, used

oils, acid oils, and fatty acid distillates. Using these feedstocks for enzymatic biodiesel production is sound, not only from a technical perspective, but also economically and from a sustainability standpoint as well.

“Enzymatic biodiesel production using bioethanol and waste oils could become a ‘green-green’ biodiesel for the future,” says Per Munk Nielsen, Senior Science Manager at Novozymes.

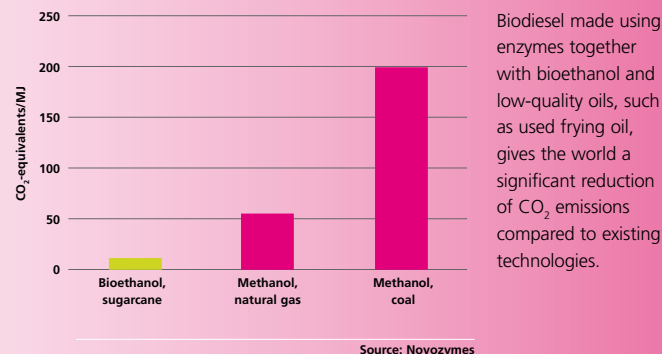
Not widespread yet

Yet, despite the obvious environmental benefits of enzymatic biodiesel production using bioethanol, the process is still not widespread.

“There are valid reasons why plants are not using this technology for commercial-scale production at this point in time,” says Jesper Brask, Science Manager at Novozymes. “It’s mainly due to the lack of an optimized process design coupled with the lack of cost-effective enzymes.”

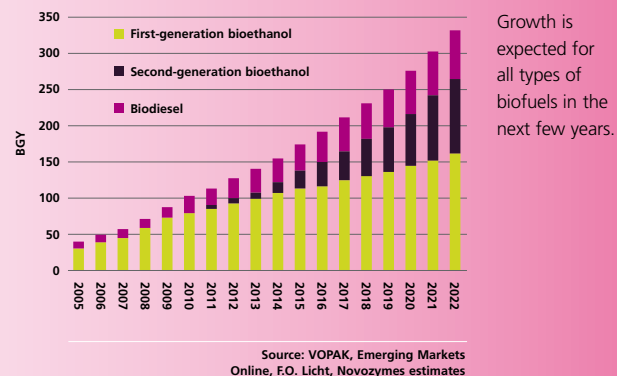
However, recent data documenting the productivity of the enzymatic process for biodiesel together with the development of new immobilization technology, which allows the reuse of the enzymes, indicate that enzyme catalysts can soon become cost-effective.

FIG. 1. ETHANOL-BASED BIODIESEL REDUCES CO₂ EMISSIONS



Biodiesel made using enzymes together with bioethanol and low-quality oils, such as used frying oil, gives the world a significant reduction of CO₂ emissions compared to existing technologies.

FIG. 2. GLOBAL BIOFUEL PRODUCTION



Growth is expected for all types of biofuels in the next few years.

Part of the future energy mix

The world faces an urgent climate change challenge – action is needed now to mitigate further damage to the planet. Boosting the amount of renewable liquid fuels of all types is key to reducing global CO₂ emissions.

The US is a major user of gasoline and consumes a smaller proportion of diesel for its transport fuel needs than other regions of the world. But Europe, China, India, and Brazil have a larger proportion of their transportation needs tied to diesel.

“A greener biodiesel solution will positively affect large areas of the world and is a very important part of a cleaner energy mix,” says Hans Christian Holm. ■

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PUTTING BIOTECHNOLOGY INTO BIOPHARMACEUTICALS

Novozymes Biopharma is well positioned to enable companies to develop superior biopharmaceutical drugs, which represent a third of the drugs currently in the global pharmaceutical development pipeline.

The pharmaceutical industry has been growing at a rate of more than 8% a year since 2003. In future, there are signs of continued growth driven by aging populations, demand for ever-improving healthcare, and the expanding markets in emerging countries.

As people live longer in developed countries, the percentage of the population consisting of elderly people is increasing. For example, more than one in five of the population in Japan, Italy, France, and Germany will be 65 years or older by 2020 (see Fig. 1). An aging population has a significantly greater need of healthcare and so represents a big potential market for pharmaceuticals.

Meanwhile, in emerging countries, sections of the population are demanding the kind of healthcare standards found in the richer countries. India, for example, has a growing middle class with high spending power. Diet is changing too – sometimes for the worse. As Indians move away from their traditional foods, the prevalence of type 2

diabetes is soaring, caused by poor diet and lack of exercise. About two thirds of all cases worldwide are now found in the Asia Pacific region with China alone having 40 million sufferers.

Type 2 diabetes is just one of the metabolic diseases that is increasing around the world. Obesity is also rising, and according to one estimate, two out of three Americans are overweight or obese and 12% of US healthcare costs is related to obesity.

Role of biopharmaceuticals

Here are some of the treatment areas targeted for future growth by pharmaceutical companies:

- Obesity/diabetes/metabolic diseases
- Alzheimer’s disease & memory
- Antiaging
- Anti-infectives (because of rising antibiotic resistance)
- Wellness (preventive/predictive cure)

Many new treatments will be based on biopharmaceuticals, not conventional synthetic drugs developed by chemical routes. Biopharmaceuticals have the advantage that they can be specifically targeted towards a particular disease or area of the body. Biopharmaceuticals constitute 11% of the current drugs on the market and 32% of all drugs under development. The drug development process, however, is long and expensive: The average time for development is 12 years, and the average cost is USD 1.2 billion.

Not surprisingly, the biopharmaceutical industry is seeking to reduce costs and the time to market. Novozymes Biopharma is uniquely positioned to address the needs of this industry through its innovative products and technologies. These improve the safety and stability of a drug product while streamlining drug development.

One solution for the future is the development of single reliable host expression and manufacturing platforms to produce a number of molecule entities across a biotherapeutics portfolio including proteins, peptides, antibodies, domain antibodies, etc. Such systems can help to lower production costs in commercial-scale manufacturing.

Formed in 2007

Novozymes has huge knowledge and expertise developed over the years in the industrial biotech field. The company is ranked as the seventh largest biotech company in the world in terms of sales and is best known as the market leader in industrial enzymes. Novozymes Biopharma was formed in 2007 to become a dedicated force within Novozymes for serving the pharmaceutical industry. Novozymes’ core capabilities in recombinant protein production and large-scale biotech processes are equally applicable to the production of biopharmaceuticals as to the production of enzymes.

Novozymes supports pharmaceutical companies with innovative recombinant products and technologies. Novozymes Biopharma also has a large manufacturing capacity with cGMP (cur-

HOW NOVOZYMES’ PRODUCTS AND TECHNOLOGIES FIT IN WITH THE CUSTOMER’S PROCESS



rent good manufacturing practice) capabilities around the world in Denmark, Sweden, the UK, and China (under construction). For example in the UK, Novozymes has developed its own safe and reliable high-yielding yeast expression systems that can be outlicensed or used for contract manufacturing.

Novozymes Biopharma operates in four main areas:

- *Recombinant albumin* is used in drug formulation to make better drugs and medical devices
- *Albumin fusion technology* for extended drug half-life and greater compliance
- *Hyaluronic acid* is used to make superior drugs and medical devices
- *Various recombinant proteins plus Protein A* for better drug production in mammalian cell culture

The different areas are unified by leveraging Novozymes’ industrial microbial biotechnology capabilities and biopharma insight.

Recent successes

In the last 12 months, there have been some notable successes.

In August 2008, Novozymes Biopharma launched CellPrime® rTransferrin AF – the world’s first microbially expressed recombinant human transferrin made to cGMP standards. The new product provides an animal-free alternative to current products used in mammalian cell culture for the production of biopharmaceuticals.

Then CellPrime rAlbumin AF-G was launched in April 2009. This supplement is used in large-scale mammalian cell culture for biopharma-

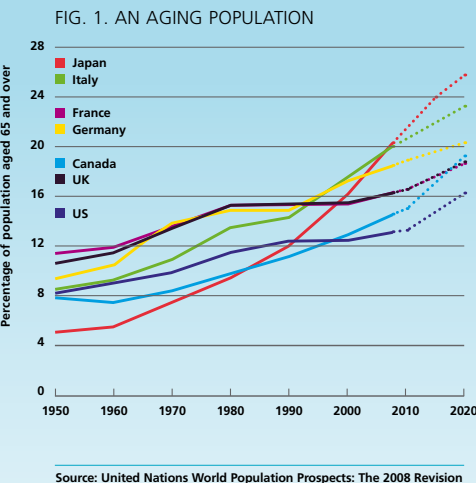
ceutical production and is produced under ISO certification.

In addition, a licensing and collaboration agreement was signed in December 2008 with sanofi-aventis for the further development and marketing of the antimicrobial peptide plectasin. The drug candidate Plectasin NZ2114/SAR215500, discovered by Novozymes in 2002, targets the treatment of severe infections such as pneumonia and septicemia caused by *Staphylococcus* and *Streptococcus*. This is the first drug candidate that Novozymes has outlicensed for further preclinical and clinical development. The expertise of sanofi-aventis in the development, marketing, and sales of pharmaceuticals complements Novozymes’ expertise in protein discovery, gene modification, and the expression of proteins and peptides. Plectasin comes from the fungus *Pseudoplectania nigrella*. It was isolated from other proteins secreted by the fungus using the screening and selection procedures refined by Novozymes for use in its enzyme business area.

Another recent deal was with ConjuChem for the supply of Recombumin®, the world’s first commercial animal-free recombinant human albumin approved for use in the manufacture of human therapeutics.

New cGMP HA facility

In April 2009, Novozymes conducted the groundbreaking for a dedicated new cGMP facility in Tianjin in China for the production of pharmaceutical-grade hyaluronic acid (HA). HA is a polysaccharide that occurs naturally in the body and is found in certain tissues. It has exceptional water-binding and remarkable viscoelastic properties, making it useful as an excipient in drugs and



medical devices. Production of pharmaceutical-grade HA will start in 2011 but pilot process samples are already available.

A growing market

Novozymes Biopharma is in a strong position to benefit from the growing wave of biopharmaceuticals by supplying and partnering with companies that produce this type of drug. The goal is to build a world-class business that will impact the biopharmaceutical world by delivering innovative solutions. Novozymes Biopharma aims to carve a niche for itself as a leading provider of recombinant products and technologies. Recent successes show that it is already on the way. ■

Novozymes is a name for biopharmaceutical companies to look out for.

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At the beginning of May, Novozymes launched a completely renovated version of the online enzyme ordering website – the Customer Center. Entirely new functionalities along with better information retrieval and ordering capabilities are among the improvements customers welcome.

THE NEW CUSTOMER CENTER IS ONLINE

Ordering Novozymes' enzyme products has become much easier. The new Customer Center lets you search for your product by name, which is much quicker than scanning a long list of items. You can also see previously ordered products and place them in your shopping cart with one click or, if you always order the same products, you can place them all in your cart at once – again with one click. It does not get much easier to order online.

Besides a streamlined ordering process, new functionalities have been added that meet customers' wishes:

- Find product documentation quickly
- Make changes to "Open" orders
- Print invoices

Using customers' suggestions

Quite a few customers were recruited to test the website and give constructive feedback. And many of the suggestions received were incorporated in the design.

"We wanted to make the Customer Center a website that truly meets its users' needs, so we used as many of our customers' requests and suggestions as possible," says Thomas Lund, CRM Manager at Novozymes. "We asked a number of our long-term customers, who've used the Customer Center over the years, to evaluate the

new website early in the design process. We made quite a few changes to our existing plans, based on the responses we received."

A great web shop experience

Early comments from users seem to show that they are satisfied with the changes made. A few customer comments tell a lot:

- "It's easy to find the information I need"
- "I like that I can sort products alphabetically. It helps me find my products quicker"
- "I like how the website looks. It's original and represents Novozymes well"

"All in all it seems that users are finding that the new Customer Center gives them a great web shop experience. That's really what we'd hoped for," says Thomas Lund. ■

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